ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
DOI: 10.1016/j.jcin.2010.09.017

Prediction of 1-Year Clinical Outcomes Using the SYNTAX Score in Patients With Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

A Substudy of the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) Trials

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Objectives This study sought to evaluate the impact of SYNTAX score (SXscore), and compare its performance in isolation and combination with the PAMI (The Primary Angioplasty in Myocardial Infarction Study) score, for the prediction of 1-year clinical outcomes in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention.

Background Patients with STEMI were excluded from the original SYNTAX score (SXscore) algorithm. Therefore, the utility of using the SXscore in this patient group remains undefined.

Methods SXscore was calculated retrospectively in 807 patients with STEMI enrolled in the randomized STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) clinical trials. Clinical outcomes of all-cause death, reinfarction, and clinically driven target vessel revascularization were subsequently stratified according to SXscore tertiles: $SX_{LOW} \leq 9$ (n = 311), $9 < SX_{MID} \leq 16$ (n = 234), $SX_{HIGH} > 16$ (n = 262).

Results At 1-year follow-up, all clinical outcomes including mortality, mortality/reinfarction, major adverse cardiac events (MACE) (a composite of all-cause death, reinfarction and target vessel revascularization), and definite, definite/probable, and any stent thrombosis were all significantly higher in patients in the highest SXscore tertile. SXscore was identified as an independent predictor of mortality, MACE, and stent thrombosis out to 1-year follow-up. The combination SYNTAX-PAMI score led to a net reclassification improvement of 15.7% and 4.6% for mortality and MACE, respectively. The C-statistics for the SXscore, PAMI score, and the combined SYNTAX-PAMI score were 0.65, 0.81, and 0.73 for 1-year mortality, and 0.68, 0.64, and 0.69 for 1-year MACE, respectively.

Conclusions SXscore does have a role in the risk stratification of patients with STEMI having primary percutaneous coronary intervention; however, this ability can be improved through a combination with clinical variables. (Multicentre 2×2 Factorial Randomised Study Comparing Tirofiban Versus Abciximab and SES Versus BMS in AMI; NCT00229515) (J Am Coll Cardiol Intv 2011;4:66–75)

Currently, several validated patient-based risk scores are in use in patients presenting with ST-segment elevation myocardial infarction (STEMI) (1–5). Most of these scores, apart from the Zwolle and CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications) scores, rely entirely on patient-based variables such as Killip class, serum creatinine levels, and degree of ST-segment change. This is not surprising given these models were developed before the widespread use of primary percutaneous coronary intervention (PCI) for the treatment of STEMI. Overall, the individual ability of these scores to predict mortality is somewhat variable (6), and a notable limitation is the absence of any assessment of lesion characteristics.

The SYNTAX score (SXscore) is an angiographic scoring system that has been shown to be able to aid revascularization decisions, and predict mortality and morbidity in patients irrespective of disease severity, at both short- and long-term follow-up (7–15). These previous assessments of the SXscore have been largely limited to elective patients. At present, therefore, the SXscore has not been validated in patients with STEMI, and as such, the utility of risk stratifying these patients using the SXscore remains unknown.

The objective of this study was to assess the impact of the SXscore and compare its performance in isolation, and in combination, with an entirely clinical-based score, the PAMI (Primary Angioplasty in Myocardial Infarction) study score, for the prediction of 1-year clinical outcomes in patients with STEMI treated with primary PCI, who were enrolled in the prospective randomized STRATEGY (Single High Dose Bolus Tirofiban and Sirolimus Eluting Stent Versus Abciximab and Bare-Metal Stent in Myocardial Infarction) (16) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction) (17) studies.

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Manuscript received August 2, 2010; accepted September 3, 2010.

Methods

Study population. The STRATEGY and MULTISTRATEGY studies have been published previously (16,17). In brief, the single-center prospective STRATEGY study randomized 175 patients to treatment with either tirofiban and sirolimus-eluting stents (SES) or abciximab and bare-metal stents (BMS), whereas the multicenter MULTISTRATEGY study randomized 745 patients between an infusion of either tirofiban or abciximab and stenting with either a SES or BMS.

Patient selection. Inclusion and exclusion criteria were similar for both studies. Patients presenting with STEMI who had: 1) chest pain for >30 min with ST-segment elevation of ≥1 mm in ≥2 contiguous electrocardiographic leads or with presumably new left bundle-branch block; and 2) admission either <12 h of symptom onset or between 12 and 24 h with evidence of continuing ischemia were eligible for enrollment. Exclusion criteria included administration of fibrinolytic agents in the previous 30 days, history of bleeding diathesis or allergy to the study drugs, major surgery within 15 days, and active bleeding or previous stroke in the last 6 months. The institutional review board at each participating center approved the protocol, and all patients gave written informed consent.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
IRA = infarct-related artery
MACE = major adverse cardiac event(s)
PCI = percutaneous coronary intervention
ROC = receiver-operator characteristic
SES = sirolimus-eluting stent(s)
ST = stent thrombosis
STEMI = ST-segment elevation myocardial infarction
SXscore = SYNTAX score
TIMI = Thrombolysis In Myocardial Infarction
TVR = target vessel revascularization

Randomization and procedure. Detail information regarding the randomization procedure for both studies is provided elsewhere (16,17). In brief, before angiography open-label 1:1 and 1:1:1:1 randomization was performed in the STRATEGY and MULTISTRATEGY studies, respectively. In STRATEGY, patients were randomized to an infusion of tirofiban and then PCI with SES or an infusion of abciximab followed by PCI with BMS. In MULTISTRATEGY, patients were randomized to an infusion of tirofiban or abciximab followed by PCI with either SES or BMS. Tirofiban and abciximab were administered before sheath insertion. Crossover to a BMS was only allowed when SES implantation failed or when it was impossible to match SES diameter with coronary reference diameter.

Details of angiographic and electrocardiographic analysis together with dosage regimes of the parenteral periprocedural anticoagulants heparin, tirofiban, and abciximab are provided elsewhere (16,17). All patients received aspirin

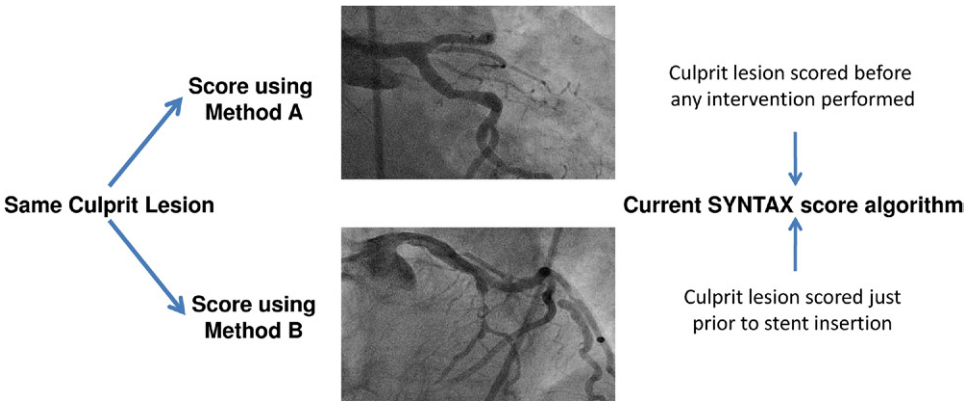

Figure 1. Schematic Diagram Indicating the Different Scoring Methods Used to Calculate the SYNTAX Score of the Culprit Lesion

Each culprit lesion was scored using Method A, where the lesion SYNTAX score was calculated before any instrumentation of the vessel, and then using Method B, where the lesion SYNTAX score was calculated using the angiographic film just before stent implantation. In this example, both images are of the same lesion in the left anterior descending artery; on the initial angiographic films **(top)** the left anterior descending artery was occluded, following wiring, and before dilation **(bottom)**, an open vessel was seen with an underlying bifurcation lesion. Therefore, the lesion was scored as an acute occlusion using Method A, and a bifurcation lesion using Method B. The results of the scores calculated using Method B are available in the Online Appendix.

Table 1. Baseline Characteristics of the Patients Stratified Into SYNTAX Score Tertiles

Variable	SYNTAX Score ≤9 (n = 311)	SYNTAX Score >9–16 (n = 234)	SYNTAX Score >16 (n = 262)	p Value
Baseline characteristics				
Age, yrs	61.8 ± 11.9	63.3 ± 11.1	66.1 ± 11.7	<0.001
Male	234 (75.2)	183 (78.2)	191 (72.9)	0.39
Risk factors				
Diabetes	32 (10.3)	29 (12.4)	49 (18.7)	0.01
Hypertension	170 (54.8)	128 (55.2)	156 (59.8)	0.69
Hyperlipidemia	130 (41.8)	88 (37.8)	103 (39.5)	0.91
Current cigarette use	131 (42.1)	92 (39.5)	84 (32.4)	0.07
Creatinine clearance, ml/min				0.003
Median	80.7	81.1	73.1	
IQR	63.5–102.6	61.7–102.4	55.3–94.3	
Prior myocardial infarction	17 (5.5)	20 (8.6)	27 (10.3)	0.33
Prior percutaneous coronary intervention	13 (4.2)	10 (4.3)	13 (5.0)	0.88
Prior stroke or transient ischemic attack	7 (2.3)	13 (5.6)	14 (5.3)	0.13
Left ventricular ejection fraction*				
Median	50	45	42	<0.001
IQR	45–55	40–52	35–50	
Killip class ≥II	30 (9.7)	32 (13.9)	55 (21.2)	<0.001
Heart rate, beats/min				
Median	72	75	75	0.06
IQR	60–85	62–89	66–89	
Time from onset of symptoms to hospital presentation, min				
Median	110	120	107	0.23
IQR	61–180	65–207	65–196	
Time from hospital presentation to angioplasty, min†				
Median	87	80	90	0.31
IQR	60–122	57–120	60–126	

Values are n (%) or mean ± SD, unless otherwise stated. *Assessed at standard transthoracic echocardiogram at discharge; †calculated as the time difference between first hospital contact and first balloon inflation.

IQR = interquartile range.

(160 to 325 mg orally or 250 mg intravenously, followed by 80 to 125 mg/day orally indefinitely) and clopidogrel (300 mg orally and then 75 mg/day for at least 3 months).

SYNTAX score. SXscore for each patient was calculated retrospectively by scoring all coronary lesions with a diameter stenosis ≥50%, in vessels ≥1.5 mm, using the SXscore algorithm, which is described in full elsewhere (7,11) and is available on the SXscore website (18). All angiographic variables pertinent to SXscore calculation were computed by 2 investigators blinded to clinical outcomes (S.G., G.S.). In the event of disagreement, the opinion of a third investigator was sought, and the final decision was made by consensus.

There is currently no validated method of calculating the SXscore in patients with STEMI as this patient group was excluded from the initial SXscore algorithm (7). To overcome this, 2 different methods of scoring the infarct-related artery (IRA) were investigated in this study. The first

Table 2. Procedural Results and Use of Medications Stratified Into Tertiles of the SYNTAX Score

Variable	SYNTAX Score ≤9 (n = 311)	SYNTAX Score >9–16 (n = 234)	SYNTAX Score >16 (n = 262)	p Value
Extent of disease				<0.001
Single-vessel disease	195 (62.7)	111 (47.4)	84 (32.1)	
Double-vessel disease	97 (31.2)	84 (35.9)	90 (34.4)	
Triple-vessel disease	19 (6.11)	39 (16.7)	88 (33.6)	
Infarct-related vessel				<0.001
Left anterior descending coronary artery	87 (28.1)	104 (44.8)	169 (65.0)	
Left circumflex artery	71 (22.9)	37 (16.0)	25 (9.6)	
Right coronary artery	151 (48.7)	90 (38.8)	63 (24.2)	
Left main coronary artery	1 (0.3)	1 (0.4)	3 (1.2)	
Lesion characteristics				
Number of diseased lesions				
Median	1	2	3	<0.001
IQR	1–2	1–3	2–4	
Range	1–4	1–6	1–7	
≥1 bifurcation lesion	67 (21.5)	119 (50.9)	184 (70.2)	<0.001
≥1 occlusion	120 (38.6)	144 (61.5)	210 (80.2)	<0.001
≥1 tortuous lesion	22 (7.1)	23 (9.8)	43 (16.4)	<0.001
≥1 lesion ≥20 mm	70 (22.5)	91 (38.9)	138 (52.7)	<0.001
≥1 calcified lesion	7 (2.3)	22 (9.4)	67 (25.6)	<0.001
≥1 lesion with thrombus	65 (20.9)	64 (27.4)	64 (24.4)	0.21
Procedural characteristics				
Number of stents implanted in the culprit lesion				
Median	1	1	1	0.004
IQR	1–1	1–1	1–1	
Range	0–3	0–4	0–4	
Total length of stent in the culprit lesion, mm				
Median	18	23	22	<0.001
IQR	18–23	18–28	18–28	
Incomplete revascularization	97 (31.2)	159 (67.9)	210 (80.2)	<0.001
Abciximab therapy*	149 (47.9)	119 (49.2)	125 (47.7)	0.56
Tirofiban therapy†	162 (52.1)	115 (50.9)	137 (52.3)	
Use of intra-aortic balloon pump	0 (0)	3 (1.3)	14 (5.4)	<0.001
Medications at discharge‡				
Number evaluated	309	229	254	
Aspirin	299 (96.8)	222 (96.9)	244 (96.1)	0.39
Clopidogrel or ticlopidine	292 (94.5)	224 (97.8)	245 (96.4)	0.71
Beta-blockers	242 (78.3)	182 (79.5)	200 (78.7)	0.90
Statins	270 (87.4)	196 (85.6)	216 (85.0)	0.82
ACE inhibitors	238 (77.0)	179 (78.2)	203 (79.9)	0.89

Values are n (%) or mean ± SD, unless otherwise stated. *Two patients who were randomized to abciximab were mistakenly treated with tirofiban; †1 patient randomized to tirofiban received both tirofiban and abciximab; ‡differences in the numbers of patients who were evaluated are due to the deaths of patients before discharge.

ACE = angiotensin-converting enzyme; other abbreviations as in Table 1.

method (Method A) involved calculating the SXscore using the current algorithm, with the culprit lesion scored using the angiographic views of the IRA before any intervention. Therefore, if the IRA was occluded it was scored as an occluded artery of <3-months' duration. The second method (Method B) still used the current scoring algorithm; however, the angiographic films just before stent implantation were used to score the culprit lesion (Fig. 1). Clinical outcomes according to the SXscore calculated using Method B, and a comparison of the 2 different scoring methods is reported in the Online Appendix; the SXscores calculated using Method A are presented in the rest of this article.

PAMI score. The PAMI score was selected as a comparative risk score as only clinical variables such as patient age, Killip class, heart rate, diabetic status, and location of myocardial infarction are required for its calculation, in contrast to the angiographic variable used in the SXscore. The PAMI score was calculated retrospectively using algorithms that are described in detail elsewhere (1). A combination of the SXscore (calculated using Method A) and the PAMI score, the SX-PAMI score, was also created as described in the Online Appendix.

Study end points. The primary end point of this post hoc study was mortality at 1-year follow-up. Secondary end points included: reinfarction; clinically driven target vessel revascularization (TVR), major adverse cardiac events (MACE) (a composite of death, reinfarction, and TVR), and stent thrombosis (ST) out to 1-year follow-up. An independent blinded clinical events committee evaluated all clinical end points, and a data and safety monitoring board ensured the safe conduct of the trial.

Definitions. Complete definitions are provided elsewhere (16,17). Deaths from all causes are reported. Re-infarction was defined as: 1) ≤24 h of randomization: recurrent ischemic symptoms with new, persistent ST-segment elevation ≥1 mm in ≥2 contiguous leads or new persistent ST-segment depression ≥1 mm in ≥2 contiguous leads not due to changes from evolution of the index STEMI; 2) between 24 h and 7 days of randomization: ischemic symptoms ≥20 min and either a creatinine kinase level ≥twice the upper limit of normal or further elevations ≥50% above the previous lowest level in patients with already elevated enzyme levels; and 3) after 7 days of randomization: either a typical increase and decrease of levels of biochemical markers of myocardial necrosis to greater than the upper limit of normal or, if markers are already elevated, further elevation of a marker ≥50% of the lowest recovery level from the index STEMI with either ischemic symptoms or other ischemic changes on the electrocardiogram. Clinically driven TVR was defined as any coronary artery bypass graft surgery, or a second PCI of the original target vessel, driven by clinical symptoms of myocardial ischemia with either a positive stress test or electrocardiographic evidence of ischemic changes at rest attributable to the target vessel and the presence of luminal stenosis of ≥70% of the reference luminal diameter by visual estimate. A successful PCI was defined as a residual stenosis <30% in the treated vessel with Thrombolysis In Myocardial Infarction (TIMI) coronary flow grade 3. Stent thrombosis was classified according to the Academic Research Consortium classification (19).

Statistical analysis. All analyses were conducted according to the intention-to-treat principle. All variables were stratified according to SXscore tertiles. Discrete data were summarized as frequencies (%), whereas parametric continuous data were expressed as mean ± SD, and nonparametric continuous data were expressed as median (interquartile range). The Fisher exact test (categorical variables), 1-way analysis of variance test (parametric, continuous variables), and Kruskal-Wallis test (nonparametric, continuous variables) were used to analyze differences between the 3 study

Table 3. Clinical Outcomes at 12 Months Stratified Into Tertiles of the SYNTAX Score

Outcome	SYNTAX score ≤9 (n = 311)	SYNTAX score >9–16 (n = 234)	SYNTAX Score >16 (n = 262)	p Value
Hierarchical outcomes at 1 yr	(n = 311)	(n = 234)	(n = 262)	
Death	10 (3.2)	10 (4.3)	24 (9.2)	0.006
Reinfarction	4 (1.3)	6 (2.6)	16 (6.1)	
Death or reinfarction	14 (4.5)	16 (6.8)	40 (15.3)	<0.001
MACE*	24 (7.7)	31 (13.2)	65 (24.8)	<0.001
Nonhierarchical outcomes at 1 yr				
Reinfarction	4 (1.3)	7 (3.0)	18 (6.9)	0.001
Target vessel revascularization	11 (3.5)	17 (7.3)	32 (12.2)	0.001
Definite ST	1 (0.3)	2 (0.9)	10 (3.8)	0.002
Definite or probable ST	2 (0.6)	5 (2.1)	14 (5.3)	0.001
Definite or probable or possible ST	4 (1.3)	7 (3.0)	18 (6.9)	0.001

Values are n (%). *A composite of death, reinfarction and target vessel-revascularization.
MACE = major adverse cardiac events; ST = stent thrombosis; other abbreviations as in Table 1.

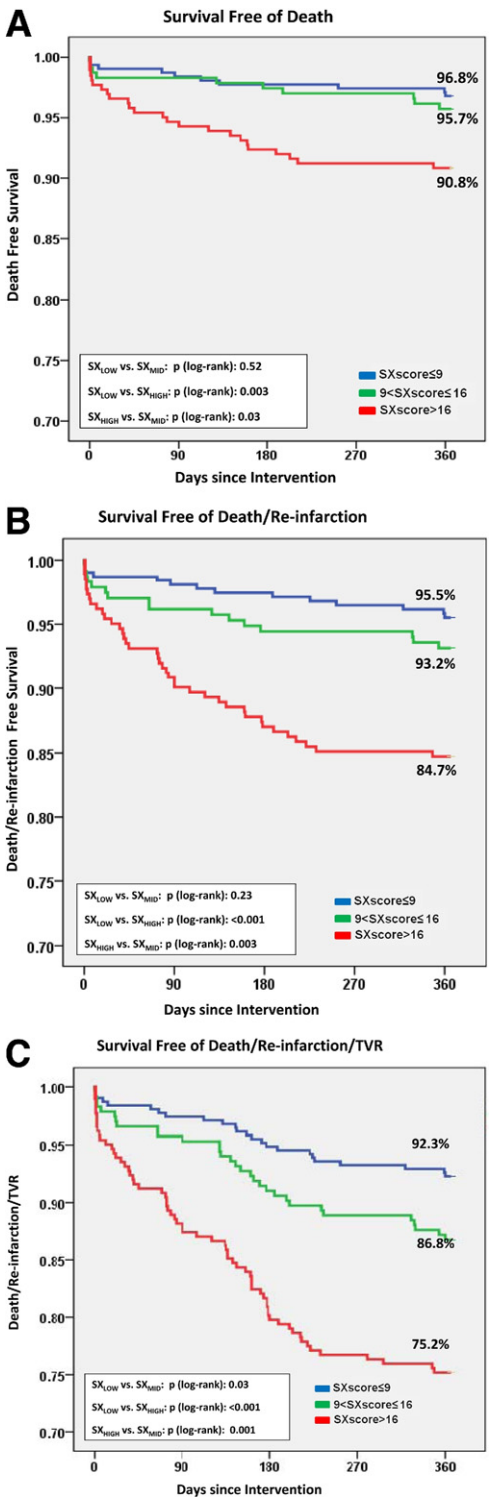

Figure 2. Kaplan-Meier Survival Curves

Kaplan-Meier survival curves for **(A)** death; **(B)** the composite of death and reinfarction, and **(C)** the composite of death, re-infarction and target vessel revascularization. Patients in the highest SYNTAX score tercile have significantly poor outcomes compared to those in the lower 2 terciles.

groups. Event-free survival curves were generated by the Kaplan-Meier method, and survival between groups was compared using the log-rank test. Cox regression analysis was used to find independent predictors of mortality, MACE, and any ST with those variables with a p value of <0.10 in the univariate analysis being included in the backward stepwise multivariate model. A reclassification analysis was used to compare the SXscore calculated by Methods A and B, and the SXscore with the SX-PAMI score, as described in the Online Appendix. Receiver-operator characteristic (ROC) curves were used to compare the discrimination of the SXscore, PAMI score, and SX-PAMI score. A 2-sided p value <0.05 was considered significant for all tests. All analyses were performed using SPSS software (version 17.0, SPSS, IBM, Somers, New York).

Results

In total, the STRATEGY and MULTISTRATEGY studies enrolled 945 patients. The SXscore was subsequently calculated in 807 (85.4%) patients (1,584 lesions); the primary reasons for the incomplete dataset were missing angiogram compact discs and the presence of coronary artery bypass grafts.

SYNTAX score. SXscore ranged from 0 to 66, with a mean ± SD of 13.9 ± 8.6 and a median (interquartile range) of 12.3 (11.4). SXscore was not normally distributed (Kolmogorov-Smirnov $p < 0.05$). In this post hoc analysis, patients were stratified according to approximate SXscore tertiles defined as: $SX_{LOW} \leq 9$ (n = 311), $9 < SX_{MID} \leq 16$ (n = 234), $SX_{HIGH} > 16$ (n = 262).

Baseline clinical angiographic and procedural characteristics. Baseline clinical, angiographic, and procedural characteristics stratified according to SXscore tertile are summarized in Tables 1 and 2. Patient age and the incidence of diabetes were both significantly higher, whereas left ventricular function and creatinine clearance were both significantly lower in the SX_{HIGH} tertile. In line with its method of derivation, markers of increased lesion complexity such as the presence of bifurcation lesions and total occlusions were all significantly higher in the SX_{HIGH} tertile.

Clinical outcomes. Clinical outcomes through to 12-months follow-up are shown in Table 3, whereas Kaplan-Meier cumulative curves are shown in Figure 2. Overall, all clinical outcomes including the primary end point of all-cause death; the composite of death/reinfarction; MACE; and rates of definite, definite/probable, and any ST were all significantly higher in the highest SXscore tertile.

Multivariate analysis. The results of the Cox multivariate analysis for death, the composite of MACE and any ST are shown in Table 4. Following multivariate adjustment, the SXscore remained an independent predictor of death, MACE, and any ST at 1-year follow-up.

Table 4. Univariate and Multivariate Predictors of Death, MACE, and Any ST

	Univariate Predictors		Multivariate Predictors	
Variable	HR (95% CI)	p Value	HR (95% CI)	p Value
Death				
Creatinine clearance	0.97 (0.96–0.98)	<0.001		
Left ventricular function	0.92 (0.89–0.94)	<0.001	0.95 (0.92–0.98)	0.003
Male sex	0.51 (0.28–0.94)	0.03		
PAMI score	1.34 (1.24–1.47)	<0.001	1.15 (1.00–1.09)	0.03
SYNTAX score	1.05 (1.03–1.08)	<0.001	1.05 (1.00–1.09)	0.02
Major adverse cardiovascular events				
Creatinine clearance	0.99 (0.98–1.00)	0.01		
Door-to-balloon time	1.01 (1.00–1.02)	0.02		
Left ventricular function	0.94 (0.92–0.96)	<0.001	0.97 (0.95–0.99)	0.001
PAMI score	1.17 (1.10–1.23)	<0.001	1.09 (1.00–1.18)	0.045
Sirolimus-eluting stent use	0.55 (0.38–0.80)	0.002	0.64 (0.43–0.98)	0.04
SYNTAX score	1.06 (1.04–1.08)	<0.001	1.07 (1.04–1.10)	<0.001
Any stent thrombosis				
Left ventricular function	0.91 (0.87–0.96)	<0.001	0.95 (0.91–0.99)	0.02
PAMI score	1.25 (1.12–1.39)	<0.001	1.13 (0.97–1.30)	0.11
SYNTAX score	1.07 (1.04–1.10)	<0.001	1.06 (1.02–1.11)	0.008

CI = confidence interval; HR = hazard ratio; PAMI = Primary Angioplasty in Myocardial Infarction; other abbreviations as in Tables 1 and 3.

SXscore calculated using Method B. Clinical outcomes and the results of a Cox multivariate analysis using the SXscore calculated using Method B are reported in the Online Appendix, Online Tables 1 and 2, and Online Figure 1. To compare both methods of SXscoring, a reclassification analysis was also performed and this demonstrated that compared with Method A, the SXscore calculated using Method B inappropriately reclassified over 12% of patients for the end point of mortality, and just under 1% of patients for the end point of MACE. The results of this reclassification analysis are provided in full in the Online Appendix and Online Tables 3 and 4.

SXscore versus PAMI score. The PAMI score was available in 791 patients and ranged from 0 to 14, with a mean ± SD of 3.9 ± 3.3 and a median (interquartile range) of 3 (5). On Cox multivariate analysis, the PAMI score was an independent predictor of mortality and MACE out to 1-year follow-up; however, unlike the SXscore, it was only a univariate predictor of any ST. The ROC curves and the respective C-statistics for the SXscore calculated using Methods A and B, the PAMI score, and SX-PAMI score for 1-year mortality, mortality/reinfarction, TVR, and MACE are shown in Figure 3.

SX-PAMI score. A reclassification analysis was performed to compare the SXscore with the combination SX-PAMI score for the end points of mortality and MACE. Results are presented in full in the Online Appendix and Online Tables 5 and 6. In brief, use of the SX-PAMI lead to an overall net reclassification improvement of 15.7% and 4.6% for mortality and MACE, respectively.

Discussion

This study represents the first dedicated analysis of the SXscore in patients with STEMI and demonstrates that the SXscore does have a utility in the assessment of patients having primary PCI, being an independent predictor of mortality, MACE, and any ST out to 1-year follow-up.

Mechanical revascularization, which is now the preferred treatment option for patients presenting with STEMI (20) is virtually always performed using PCI. It follows, therefore, that the goal of risk stratification in patients having primary PCI is not to determine appropriate treatment strategy, but more to determine the risk of adverse cardiac events after procedure that may guide discharge planning and follow-up schedule (5,21), while also serving as a means for individual operators, institutions, and regulatory bodies to access and compare performance.

The current study has demonstrated that patients with higher SXscores, irrespective of whether they are calculated using Method A or B, are at increased risk of mortality and MACE when presenting with STEMI. This is consistent with data from the assessment of patients having elective PCI (7–15), and also in line with previous studies of primary PCI that identify variables associated with higher SXscores such as TIMI flow grade <3 (21,22), and the presence of multivessel disease as significant independent predictors of MACE (23).

In this current analysis, 2 different methods of applying the SXscore were investigated as the initial SXscore algorithm did not include any specific reference to patients with

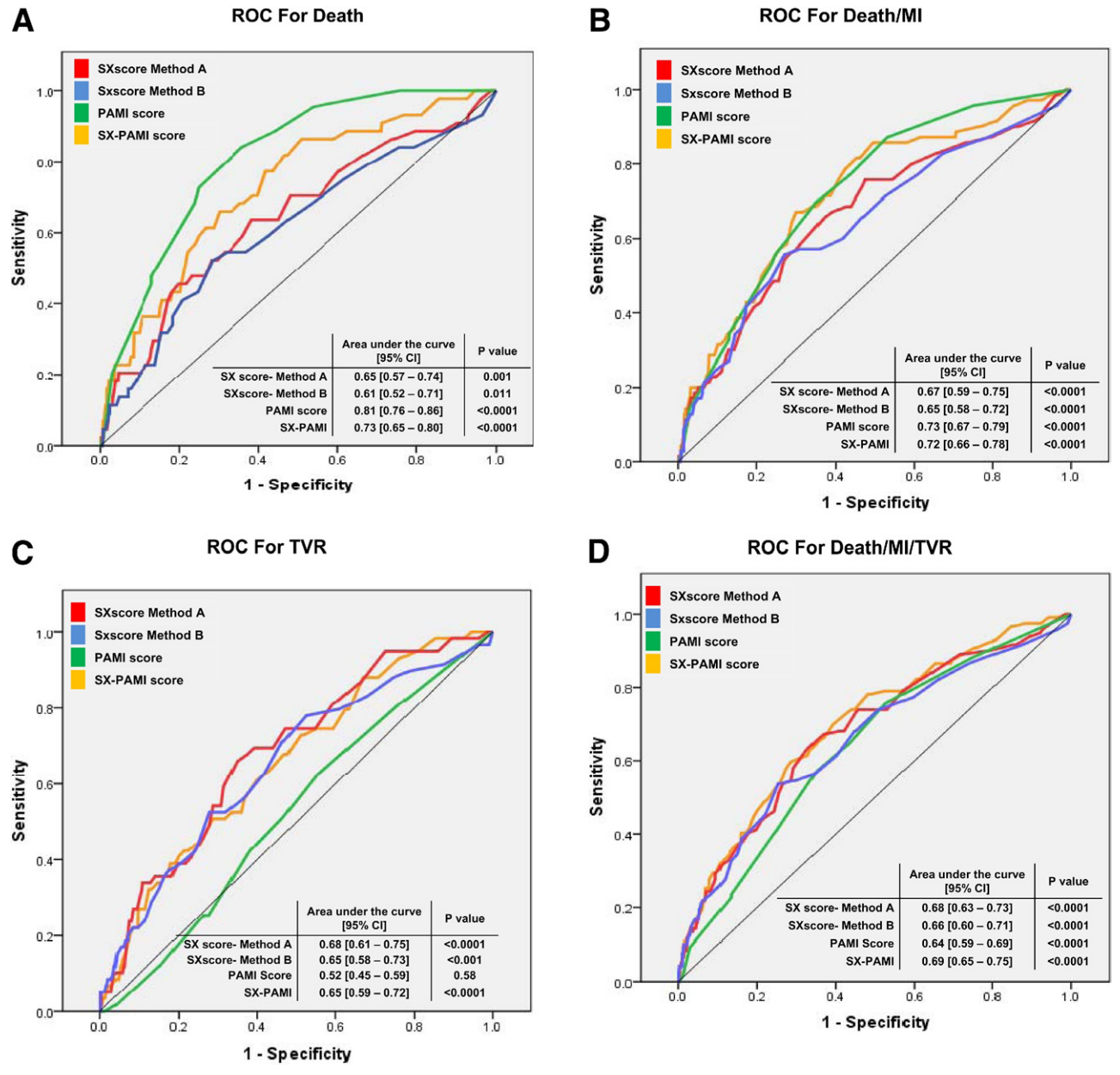

Figure 3. Receiver-Operator Characteristic Curves and Corresponding C-Statistics for the SYNTAX Score

Receiver-operator characteristic curves and corresponding C-statistics for the SYNTAX score calculated using Method A, the SYNTAX score calculated using Method B, the PAMI score and the SX-PAMI for **(A)** death, **(B)** composite of death and re-infarction, **(C)** target vessel revascularization and **(D)** the composite of death, re-infarction, and target vessel revascularization. The discriminatory ability of the SYNTAX score calculated using Method A is consistently superior to that calculated using Method B. Similarly, whilst the discriminatory ability of the SYNTAX score appears inferior to the PAMI and SX-PAMI for the assessment of death and death/re-infarction, it is superior for assessment of target vessel revascularization. The combination score, however, is superior for the assessment of the composite of death, reinfarction, and target vessel revascularization.

STEMI (7). Although both methods of scoring identified those patients at highest risk of events, and were independent predictors of clinical outcomes, there were some important differences between both scores. Of note, the SXscore calculated using Method B had an inferior discriminatory ability compared with Method A, as well as inappropriately reclassified patients with respect to the end points of death and MACE. Although both scores had the same range, the mean SXscores calculated using Method A were significantly higher than those calculated using

Method B (Method A mean: 13.9 vs. Method B mean: 10.3, $p < 0.05$). This partly reflects the weighting factor in the SXscore algorithm, which gives an occlusion-multiplying factor of 5, compared with a multiplier of 2 if the vessel has a diameter stenosis between 50% and 99%. In the setting of primary PCI, this important difference in calculation provides a possible explanation for the inappropriate reclassification observed using Method B. Patients with pre-PCI TIMI flow grade 0/1 in the IRA have been shown to have a significantly higher risk of 6-month mortality compared with those with TIMI flow grade 3 (22). It follows that this higher risk is only translated into higher SXscores calculated using Method A, when the IRA is scored as an occlusion, and not Method B. It would seem evident that the calculation of the SXscore in patients undergoing primary PCI should be performed using Method A.

One of the limitations of using the SXscore for risk stratification is the absence of clinical variables in its calculation, a deficiency that can be successfully addressed through its combination with clinical-based risk models (24,25). The present study provides additional evidence to support this: first, by demonstrating improvements in the discriminatory ability of the SXscore when combined with the PAMI score, and second, through the observed appropriate reclassification of patients following use of the combination score. Despite these modifications, the purely clinical-based PAMI score still had the greatest discriminatory ability for hard clinical end points such as mortality, indicating that these outcomes are influenced more by pre-morbid clinical characteristics than by lesion complexity. Consistent with this, Peterson et al. (26) reported only a marginal change in the C-statistic of in-hospital mortality when angiographic variables such as lesion class, vessel location, and TIMI flow grade were removed from the NCDR (National Cardiovascular Data Registry) risk score. With respect to soft end points such as TVR, the superior discriminatory ability of the SXscore may be explained by the significantly greater risk of TVR in those with incomplete revascularization (76.2% vs. 23.8%, $p = 0.007$), which in turn was significantly related to the initial SXscore.

In view of its high associated morbidity and mortality, and unpredictability, ST remains an ongoing concern following PCI, particularly following implantation of drug-eluting stent in patients with STEMI (27). The presence of thrombus can increase the risk of incomplete stent apposition, which together with delayed healing and a poorer compliance to dual antiplatelet therapy are factors implicated in increasing the risk of ST in STEMI patients (28,29). The current analysis demonstrates an important relationship between SXscore and the risk of ST, which has previously been reported in the "all-comers" LEADERS (Limus Eluted From a Durable Versus Erodable Stent Coating) population (14). Importantly, this relationship may help identify those patients who would benefit from additional measures to reduce the risk of ST such as the assessment of platelet reactivity, higher loading doses of clopidogrel, and more intensive counseling regarding compliance to dual antiplatelet therapy (30).

Study limitations. This study is limited by its post-hoc nature. The ROC method of analysis, although well suited for diagnostic purposes (31), may not be appropriate for prognostic models, because these models need to incorporate the dimension of time, which adds a stochastic element (32). Therefore, it has been suggested that ROC analysis methods are not well validated for the assessment of time-censored data; however, in the current study, the same methods have been used to assess both scoring systems, and these methods are consistent with previous published studies evaluating risk models (33). The relatively small sample size of the current study reiterates the need to validate the findings in a larger patient cohort. Unfortunately, the absence of relevant data prevented the calculation of a previously validated combined angiographic and clinical–based score such as the CADILLAC score (2). Finally, the role of calculating the SXscore after revascularization is as yet unexplored, but this may well provide important data to help determine which patients require further revascularization.

Conclusions

SXscore does have a role in the risk stratification of patients with STEMI having primary PCI; however, this ability can be improved through a combination that includes clinical variables.

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Key Words: infarct-related artery ■ major adverse cardiac events ■ percutaneous coronary intervention ■ stenting ■ stent thrombosis ■ ST-segment elevation myocardial infarction ■ SYNTAX score ■ target vessel revascularization ■ Thrombolysis In Myocardial Infarction.

APPENDIX

For supplementary methods and results, please see the online version of this article.